

**WHAT IS CLAIMED IS:**

1. A method of identifying a compound that stabilizes an  $\alpha$ -helical conformation of a discordant helix in a polypeptide, the method comprising:

- 5 (a) providing a test sample comprising a polypeptide that contains a discordant helix in the form of an  $\alpha$ -helix;
- (b) contacting the test sample with a test compound; and
- (c) determining the rate of decrease in the amount of  $\alpha$ -helix in the test sample, wherein a lower rate of decrease in the presence of the test compound than in the absence of the test compound is an indication that the test compound stabilizes the  $\alpha$ -helical
- 10 conformation of the discordant helix in the polypeptide.

2. A method of identifying a compound that can stabilize the  $\alpha$ -helical conformation of a discordant helix-containing polypeptide, the method comprising:

- 15 a) providing a test sample comprising a polypeptide that contains a discordant helix in the form of an  $\alpha$ -helix;
- b) contacting the test sample with a test compound; and
- c) determining the amount of  $\alpha$ -helix present in the test sample, wherein a higher amount of  $\alpha$ -helix remaining in the presence of the test compound than in the absence of the compound indicates that the test compound stabilizes the  $\alpha$ -helical
- 20 conformation of the discordant helix in the polypeptide.

3. A compound identified by the method of claim 1.

4. A compound identified by the method of claim 2.

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5. A method of identifying whether a protein is susceptible to forming amyloid, the method comprising analyzing the amino acid sequence of the protein to determine whether the protein contains a predicted discordant helix, wherein the presence of predicted discordant helix is an indication that the protein is susceptible to forming amyloid.

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6. The method of claim 5, wherein the discordant helix is at least six amino acids in length.

7. A method of decreasing the rate of formation of  $\beta$ -strand structures between at least two discordant helix-containing polypeptides, the method comprising contacting the discordant helix-containing polypeptides with a compound that stabilizes an  $\alpha$ -helical form of the discordant helix.

8. A method of treating an individual having or at risk for an amyloidosis, the method comprising administering to the individual a therapeutically effective amount of a compound that stabilizes an  $\alpha$ -helical form of a discordant helix-containing polypeptide that forms amyloid.

9. The method of claim 8, wherein the amyloidosis is selected from the group consisting of prion diseases and Alzheimer's disease.